

## Correspondence

EDITED BY STANLEY ZAMMIT

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### Smaller trials for better evidence

The interesting debate between Parker and Anderson & Haddad (2003) suggests more fundamental reasons to question prevailing research paradigms and designs in respect of the efficacy of and indications for psychotropic medicines. That the clinical trial industry reveals even marginal drug effects may be seen as surprising given the virtual absence of any basis for a taxonomy of mental disorders, other than the syndromal classifications used in psychiatric practice. There is little evidence that the major syndromes align with any readily defined pathophysiological variance. Group heterogeneity in trial work, as the debaters remark, will therefore attenuate the evidence for substantial drug treatment effects, sometimes to vanishing point. Meta-analysis of such data may not be much more revealing, compounding the influence of variable sampling in individual trials and publication bias.

These side-effects of the randomised controlled trial ethos are not greatly mitigated in the field of organic mental disorders. At huge expense, multicentre trials of cholinesterase inhibitors in patients classified as probably having Alzheimer's disease have shown only very modest (and to many observers still unconvincing) effects on cognitive and neuropsychiatric outcomes (e.g. Lanctôt *et al*, 2003). This is because these conditions, pace distinguished efforts at nosological definition in life, are also heterogeneous. This variability, already evident from detailed clinical and neuropsychological assessment, is further revealed by functional and structural analysis of the brain. It is these data which might best inform sampling for therapeutic trials. Studies on a smaller scale, therefore, targeting the more readily defined Lewy body dementia (e.g. McKeith *et al*, 2000) or more intensively characterised and monitored patients with Alzheimer's disease (e.g. Venneri *et al*, 2001) in both double-blind and open-label designs, can convincingly demonstrate the

nature and the modalities of efficacy using cholinesterase inhibitors. In the same way, studies of smaller groups of patients receiving treatment for depression may reveal correlations between clinical features and treatment responses that are more likely to guide the selection of therapy for individual patients (Mayberg, 2003).

Large randomised controlled trials, by submerging variation in the interest of marginal statistical significance, seem to offer limited hope of significantly improving the evidence that guides clinical practice. Studies of cognitive and pharmacological interventions might best be carried out with smaller patient groups for whom there has been detailed assessment of relevant pathophysiological and cognitive variance, as well as the manifest clinical symptoms.

### Declaration of interest

M.F.S. and A.V. have received honoraria and support for attending scientific meetings, been members of advisory boards and received research grants from companies involved in the manufacture and marketing of cholinesterase inhibitors.

**Lanctôt, K. L., Herrman, N., Yau, K. K., et al (2003)** Efficacy and safety of cholinesterase inhibitors in Alzheimer's disease: a meta-analysis. *Journal of the Canadian Medical Association*, **169**, 557–564.

**MacKeith, I. G., Del Ser, T., Spano, P. F., et al (2000)** Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. *Lancet*, **356**, 2031–2036.

**Mayberg, H. S. (2003)** Modulating dysfunctional limbic-cortical circuits in depression: towards development of brain-based algorithms for diagnosis and optimized treatment. *British Medical Bulletin*, **65**, 193–207.

**Parker, G./Anderson, I. M. & Haddad, P. (2003)** Clinical trials of antidepressant medications are producing meaningless results (debate). *British Journal of Psychiatry*, **183**, 102–104.

**Venneri, A., Shanks, M. F., Staff, R. T., et al (2001)** Cerebral blood flow and cognitive responses to rivastigmine treatment in Alzheimer's disease. *NeuroReport*, **13**, 83–87.

**M. F. Shanks** Department of Psychiatry, Faculty of Medical and Health Sciences, Private Bag 92019,

University of Auckland, New Zealand. E-mail: m.shanks@auckland.ac.nz

**A. Venneri** Department of Psychiatry, University of Hull, UK

### Pendulum management in secure services

Tilt (2003) defends himself clearly against the criticisms of Drs Exworthy & Gunn (2003). However, he does not emphasise the extent to which they have misrepresented aspects of the Tilt Report (Tilt *et al*, 2000). Specifically, Exworthy & Gunn state, following their quote from the Report concerning the relationship between security and therapy, 'one should go further because in high secure hospitals therapy in its widest sense is an integral part of security'. This virtually paraphrases the Report itself: 'Security is the responsibility of all personnel in a high security hospital and . . . good security facilitates good therapy and vice versa' (paragraph 8.2).

There also appears to be a marked absence from this debate of both historical and organisational perspectives. Rapoport (1960) suggested, in considering the institutional dynamics of therapeutic institutions, that 'disturbances were partly a function of cycles of abdication of authority, in the name of permissiveness, followed by authoritarianism to restore order'. The consequences of the report on the Ashworth Hospital inquiry (Blom-Cooper *et al*, 1992) (Ashworth at that time being an abusive, authoritarian institution) were clearly thought by Fallon *et al* (1999) to relate to a breakdown of security (permissiveness), leading to the Tilt Report (which has been perceived by many in secure services as authoritarian).

Perhaps attempting to understand this cycle more, and how it may relate to the complex (and potentially contradictory) tasks facing secure psychiatric services, might reduce the likelihood of yet more scandals, inquiries and reports in the future. Scott (1975) suggested that 'detaining custodial institutions have two aims, one therapeutic, the other custodial. These can and should be complementary, but there is a tendency for these functions to polarise out and eventually split like a living cell into two separate institutions'. The debate between Exworthy & Gunn and Tilt illustrates the recurring nature of this phenomenon.